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degussa.

Degussa Corporation
379 Interpace Parkway
P.O. Box 677
Parsippany, NJ 07054-0677

Direct: (973) 541-8047
Fax: (973) 541-8040

Shaun.Clancy@degussa.com
www.degussa.com

October 6, 2003

Document Processing Center
EPA East (Mail Code 7407M)
Attn: TSCA Section 8(e)
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20460-0001



Contain NO CBI



Dear Madam or Sir:

Enclosed are summaries of 43 toxicology studies conducted by or for Degussa AG in Germany. These summaries reflect the results of one or more studies conducted on each of 21 chemical substances. Twelve of the summaries include information which we are reporting pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA). The remaining nine studies include information that suggests that the test substance may cause adverse health or environmental effects at high exposure levels. However, because these substances are manufactured or imported in the United States only in limited quantities for use as intermediates in chemical synthesis, they do not currently present a substantial risk to health or the environment. We are therefore submitting them to EPA on a "For Your Information" basis.

These 21 summaries are being submitted pursuant to a data review that Degussa is conducting in connection with its implementation of a new computer system that will permit Degussa Corporation in the United States to access data previously available only to Degussa AG in Germany. Recognizing that a large number of these studies might need to be reported under TSCA 8(e), Degussa proactively contacted EPA in mid 2002 and proposed to review the studies in batches and submit any 8(e) reportable data to EPA within 15 business days (now 30 calendar days) of completing its review of each batch. Degussa estimated that the review would take approximately six month to complete. In a memorandum received in November 2002, the Agency concurred in this approach.

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These studies were made available to Degussa Corporation in April 2003. Degussa's toxicologists in Germany have reviewed more than 750 studies on approximately 100 chemical substances and prepared English summaries of the results of 70 studies for evaluation by scientists in the United States for reporting under TSCA Section 8(e). This submission represents Degussa's review of this first batch of studies by our scientists in Germany and the United States, which was completed on September 12, 2003. Degussa has determined that approximately 1500 studies remain to be reviewed. As we have separately informed Ms. Ann Pontius of the Toxics and Pesticides Enforcement Division, we estimate that the review of the remaining studies will take an additional nine months to complete. We will continue to submit reportable and FYI studies to EPA as our review of subsequent batches is completed.

We appreciate your attention to this matter and request your comments regarding the approach we have taken. Please do not hesitate to call me at (973) 541-8047 if you have any questions or wish to discuss this matter further.

Best regards,

A handwritten signature in black ink, appearing to read "Shaun Clancy".

Shaun F. Clancy, Ph.D.

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Total Dimensional Value
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Total Charges
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Rev. Date 12/00 (P/N 1515194-2001) Mktg. Mgmt ID #USA_GDP_E_901

Memo

To: File
From: Shaun Clancy
CC:
Date: 10/06/03
Re: TSCA 8(e) Review – 88-41-5

Two endpoints were provided by Fine Chemicals for 88-41-5 2-t-Butylcyclohexyl acetate

- Acute Oral Tox
- Acute Fish Tox with Golden Orfe

This chemical is used as an intermediate in organic synthesis and is not expected to be used in a way such that human exposure outside of an industrial setting will occur or that an environmental exposure will result. Appropriate Personal Protective Equipment is specified in the MSDS as is warnings not to allow the substance to be released. When used correctly the risk for human and environmental exposure is minimal.

The results of the oral tox study indicates possible neurotoxic effects which are probably reportable under TSCA 8(e). Given the high dose, other toxic effects and the reversibility of the possible neurotoxic effects, it is not clear that the potential effects are due to neurotoxicity. The toxicity to fish, while in the "moderate" range, does not present a significant risk because of the use pattern of the chemical. This result is probably not reportable and will be submitted on an FYI basis.

Contains No CBI

degussa.

Fax

To: Shaun Clancy
S-SR-US-EHS

Fax-No. Recipient: 001-973 541 8040

Pages (total): 22

cc: Dr. W. Mayr/FC-TME-CSM

Initial notice of Information for possible TSCA 8e submission
Cyclohexanol, 2-(1,1-dimethylethyl)-acetate / 2-tertbutylcyclohexyl acetate, CAS-No. 88-41-5

Dear Shaun,

Degussa AG
Rodenbacher Chaussee 4
63457 Hanau-Wolfgang
Germany

T +49-6181-+49 6181 59-
3900
F +49-6181-+49 6181 59-
2083

sylvia.jacobi@degussa.com

www.degussa.com

Fine chemicals
Chemicals Safety
Management

FC-TME-CSM/Dr.Jbi/sch

April 30, 2003

please find attached data obtained for the above mentioned substance for assessment of possible TSCA reportability depending on the exposure situation.

I am at your disposal for any further questions.

I attach a short summary of the data together with the German reports and an English translation of the reports.

I will be at home tomorrow and on Friday and travelling monday and tuesday. You can however reach me on my mobile: +49 171 8941496.

Best regards

Sylvia Jacobi

degussa.

Initial Notice of Information to be assessed for Possible TSCA,
Sec. 8e Reporting

Degussa AG
 Rodenbacher Chaussee 4
 63457 Hanau-Wolfgang
 Germany

T +49 6181 59-3900
 F +49 6181 59-2083

Fine chemicals
 Chemicals Safety
 Management

April 30, 2003

Name / Trade name of the Substance	Cyclohexanol, 2-(1,1-dimethylethyl)-acetate / 2-tertbutylcyclohexyl acetate
CAS-No.:	88-41-5

Human Health Effects

Environmental Effects

Degussa-Study-No.:	86-0274-DKT 88-0832-DKO
Other Source of information:	

Summary of Adverse Effects:

Human health:

Acute oral toxicity study in rats

Source, Degussa AG, unpublished report No. 86-0274-DKT

Guideline: OECD Nr. 401, non-GLP, 5 male, 5 female animals per group.

The LD50 was determined to be 6100 mg/kg bw. Dose levels tested were 2150, 3160, 3980, 5010 and 6310 mg/kg bw. At all dose levels the animals were reported to show restlessness, piloerection and respiratory symptoms 15 to 30 min after the administration of the test substance. Some animals of each dose group also revealed tonic-clonic convulsions in the first few hours after the administration of the test substance. At the same time opisthotonus, exophthalmus, tremor and sudden bleeding from nose and mouth, salivation and vocation was observed. In most animals the symptoms were reversible within 7 to 8 hours. Only in 2 animals of the high dose group the symptoms persisted up to 24 hours. Necropsy of the animals that died during the study revealed hyperaemia of the mucous membranes of the gastro-intestinal tract, discoloration of the kidney, adrenals and liver, hyperaemia of the lungs and the peritoneum and corrosion of the mucous membranes of the stomach. The surviving animals showed thickened areas of the mucous membranes of the forestomach, single animals had spotted kidneys, dark red discolouration of the adrenals and hyperaemia of the mucous membranes of the duodenum.

Environmental effects

Acute fish toxicity study in golden orfe (48 h)

degussa.

Source, Degussa AG, unpublished report No. 88-0832-DKO
Guideline: DIN 38412 part 15 non-GLP

Page 02 of 02

The 48 h LC50 was 14.9 mg/l which suggests a moderate concern for aquatic organisms.

Nature and Extent of Risk Involved:
Dependent on the exposure situation.

Information by	Date:
Dr. Sylvia Jacobi	April 30, 2003

HUELS AG
Ecotoxicology/Ecology
Dr. J.B. Scheubel/Dr. N. Scholz

Marl, 9/21/88

RESEARCH REPORT NO. F915

Degussa AG – REG No.
88 – 0832 - DKO

Re.: Ecotoxicological testing of the product 2-tert.-butylcyclohexyl acetate for its acute activity in the fish test (DIN 38412 Part 15) with golden orfes

Requested by: Dr. Scheubel Sample No.: 620/880606

The product 2-tert.-butylcyclohexyl acetate was tested for its acute action (DIN 38412 Part 15) on golden orfes over a test period of 48 hours. The study was conducted in compliance with the guidelines recommended by the OECD on good laboratory practice (glp) and the general instructions on planning, implementation and evaluation of biological test procedures according to DIN 38412 Part 1.

Marlowct EF was used to produce a master batch of the test substance.

RESULTS OF THE EVALUATION:

- 1) Highest tested concentration with no effect: 10 mg/L (product)
- 2) Lowest tested concentration with 100% effect: 20 mg/L (product)
- 3) Calculated mean effective concentration (EC 50): 14.9 mg/L (product)

Comment:

Evaluation: See attachment

Fish Test, Acute (DIN 38412 Part 15)
2-tert.-butylcyclohexyl acetate

[insert figure; mg/l → mg/L)

**Evaluation of ecotoxicological study
Linear regression analysis of 9/21/88
Sine transformation**

In charge of carrying out test: E. Pommmer
Test substance: 2-tert.-butylcyclohexyl acetate

Responsible: E. Pommmer

Test procedure: Fish test, acute (DIN 38412 Part 15)

Test date: 9/14/88
Solubilizer: Marlowet EF

Number of value pairs: 4

Analysis Result:

x (mg/L)	y (% Effect)	ln x	arcsin y
10	0	1	-1.5708
13	10	1.11394335	-0.927295218
16	60	1.20411998	-0.201357921
20	100	1.30103	1.5708
Mean value log x-values:		1.15477333	
Mean value arcsin y:			-0.181484325
Slope of the regression:		10.529	
Standard error of the regression:		0.0164	
COEFFICIENT OF CORRELATION:	0.98		
Regression equation: y = -12.3405127 + 10.5293637 *x ;			

EC 50: 14.9 mg/L (product)

Standard error of the EC 50 of: 14.3-15.4 mg/L (product)

95% confidence interval of the EC 50:

from: 13.4 to 16.5 mg/L (product)

EC 0: 10.5 mg/L

EC 100: 21 mg/L (calculated)

HUELS AG
Dekotoxikologie/Dekologie
Dr.J.B.Scheubel/Dr.N.Scholz

Mari, den 21.9.88

UNTERSUCHUNGSBERICHT Nr. F915

Degussa AG — REG-Nr.
88 - 0832 - DKO

Betr.: Dekotoxikologische Pruefung des Produktes 2-tert-Butylcyclohexylacetat auf seine Wirkung im Fischtest akut (DIN 38412 Teil 15) mit Goldorfen.

Auftraggeber: Dr. Scheubel Proben-Nr.: 620/B80606

Das Produkt 2-tert-Butylcyclohexylacetat wurde im Fischtest akut (DIN 38412 Teil 15) mit Goldorfen bei einer Testdauer von 48 Stunden auf seine Wirkung geprueft. Die Untersuchung erfolgte unter Beruecksichtigung der von der OECD empfohlenen Richtlinien zur guten Laborpraxis (glp) sowie der allgemeinen Hinweise zur Planung, Durchfuehrung und Auswertung biologischer Testverfahren nach DIN 38412 teil I. Zur Herstellung eines Stammansatzes der Pruefsubstanz wurde Marlowet EF verwendet.

ERGEBNISSE DER AUSWERTUNG:

- 1.) Hoechste gepruefte Konzentration ohne Wirkung: 10 mg/l (Produkt)
- 2.) Niedrigste gepruefte Konzentration mit 100% Wirkung: 20 mg/l (Produkt)
- 3.) Berechnete mittlere Wirkkonzentration (EC 50): 14.9 mg/l (Produkt)

Bemerkung:

Auswertung: siehe Anlage

08/23 Auswertung Dekotoxikologische Untersuchung
lineare Regressionsanalyse vom 21.9.88

Sinustransformation

5 Testdurchfuehrung: E.Pommer Verantwortlich: E.Pommer
Testsubstanz: 2-tert-Butylcyclohexylacetat

Testverfahren: Fischtest akut (DIN 38412 Teil 15)

Untersuchungsdatum: 14.9.88

Loesehilfsmittel: Marlowet EF

+49 Anzahl der Wertepaare: 4

Ergebnis der Analyse:

x (mg/l)	y (% wirkung)	ln x	arcsin y
10	0	1	-1.5708
13	10	1.11394335	-.927295218
16	60	1.20411998	.201357921
20	100	1.30103	1.5708

FC-TME-CSM Mittelwert log x-Werte: 1.15477333

Mittelwert arcsin y: -.181484325

Steigung der Regression: 10.529

Standardfehler der Regression: .0164

KORRELATIONSKOEFFIZIENT: .98

Regressionsgleichung: $y = -12.3405127 + 10.5293637 * x$;

DEGUSSA AG
EC 50: 14.9 mg/l (Produkt)

Standardfehler der EC 50 von: 14.3 bis 15.4 mg/l (Produkt)

95 % Vertrauensbereich der EC 50:

von: 13.4 bis: 16.5 mg/l (Produkt)

16:31
30-APR-2003
EC 0: 10.5 mg/l EC 100: 21 mg/l (berechnet)

schtest akut (DIN 38412 Teil 15)

tert-Butylcyclohexylacetat

+49 6181 592083 S.09/23

DEGUSSA AG FC-TME-CSM

30-APR-2003 16:32

11.011 mg/l (EC 1)

14.859 mg/l (EC 50)

20.052 mg/l (EC 99)

100

Exemplar Nr. 3

Hüls AG
-WL Ps-

Marl, den 20.10.1986

Am 23.10.86

Bericht Nr. 0747

Akute orale Toxizität von

2-Tert.-Butylcyclohexylacetat

für Ratten

von

P. Mürmann

Solange die in dieser Arbeit enthaltenen Ergebnisse nicht publiziert worden sind, dürfen sie nur mit Einverständnis der Hüls AG, WL Ps verwendet werden. Eine Vervielfältigung dieses Berichtes ist -auch auszugsweise- nicht gestattet.

36 - 02.54 - DKT

- 1 -

I Zusammenfassung:

In einer akuten oralen Toxizitätsbestimmung an männlichen und weiblichen Ratten wurde festgestellt, daß der LD₅₀-Wert von 2-tert.-Butylcyclohexylacetat bei 6100 mg/kg Körpergewicht liegt. Die behandelten Tiere waren nach 48-72 Std. frei von Vergiftungssymptomen. Die Körpergewichtsentwicklung war unbeeinflußt. Die Sektionen am Versuchsende ergaben bei einigen Tieren herdförmige Verdickungen auf der Schleimhaut des Vormagens, vereinzelt fleckige Nieren, dunkelrot gefärbte Nebennieren sowie Hyperämien der Dünndarmschleimhäute.

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- 2 -

II Allgemeines:

Prüfsubstanz: 2-tert.-Butylcyclohexylacetat

Chemische Bezeichnung: 2-tert.-Butylcyclohexylacetat

Versuchsart: akute orale Toxizität (LD_{50}) für Ratten

Versuchs-Nummer: 0747

Auftraggeber: Dr. Korfmann, Org. Abt., Hüls AG, Marl

Prüfsubstanz erhalten am: 28.08.1986

Datenblatt für Prüfsubstanz erhalten am: 22.09.1986

Versuchsbeginn: 29.09.1986

Versuchsende: 15.10.1986

Versuchsleiter: Dr. P. Mürmann

Versuchsbetreuung: Frau M. Porter, Frau R. Hamphoff-Köhler

Berichterstattung: 20.10.1986

Archivierung: Rohdaten, Protokolle, Bericht und Rückstellmuster in entsprechenden Räumen der Hüls AG, Bau 2328

- 3 -

- 3 -

III Physikalische und allgemeine Angaben zur Prüfsubstanz:

Aggregatzustand:	flüssig, cis-Verbindung neigt zur Kristallisation
Dichte (20 °C):	0,941 g/cm³
pH-Wert:	6,2
Aussehen:	farblos
Geruch:	charakteristisch
Schmelzpunkt:	25-35 °C
Siedepunkt (1013 mbar):	oberhalb 204 °C Zersetzung
Dampfdruck (112 °C):	24 hPa
Flammpunkt:	89 °C
Reinheit:	größer 99 %
Hauptverunreinigungen:	
Produktionstag:	August 86
Chargen-Nr.:	1fd. Produktion
Abweichende Lagerbedingungen:	
Erforderl. Schutzmaßnahmen:	

IV Methodik:

1) Versuchstiere und Versuchstierhaltung:

Tierart, Stamm:	Ratte, Bor: WISW (SPF TNO)
Züchter:	F. Winkelmann, 4799 Borcheln
Geschlecht:	männlich und weiblich
Mittleres Körpergewicht:	194,2 g
Tierzahl pro Dosis:	10
Kennzeichnung:	innerhalb einer Gruppe wurden die Tiere durch Anfärben des Haarkleides mit Pikrinsäure unverwechselbar gekennzeichnet
Haltung:	1 - 5 Tiere in Makrolonkäfigen Typ III
Akklimatisation:	4 - 8 Tage
Futter:	R10 Alleindiät für Ratten, Ssniff Spezialfutter GmbH, 4770 Soest, ad libitum
Wasser:	Leitungswasser ad libitum
Raumtemperatur:	20 °C ± 1 °C
Rel. Luftfeuchtigkeit:	60 % ± 5 %
Luftwechsel:	15fach / Std.
Beleuchtung:	12stündiger Licht-Dunkel-Rhythmus
Randomisierung:	anhand einer willkürlichen Zahlentabelle bei Verteilung in die Versuchskäfige

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2) Versuchsdurchführung:

Der Versuch wurde nach den von der Organisation for Economic Cooperation and Development (OECD) herausgegebenen Guidelines for Testing of Chemicals, Section 4: Health Effects, Method No. 401: Acute Oral Toxicity, vom 12. Mai 1985 durchgeführt. Das Produkt wurde durch Erwärmen im Wasserbad verflüssigt. Ober 16 Stunden nüchtern gesetzte Ratten erhielten eine einmalige orale Gabe per Schlundsonde (Volumen: 2,667-6,706 cm³/kg).

Zur Dosisfindung wurde in der Zeit vom 25.09.-09.10.86 ein Vorversuch mit geringer Tierzahl durchgeführt.

Versuchsdauer: 14 Tage

3) Beobachtungen:

Körpergewichte: Die Tiere wurden vor der Behandlung und 1, 7 und 14 Tage nach der Behandlung gewogen.

Symptome: Bis zu sechs Stunden nach der Behandlung und dann täglich wurden Eintritt, Art und Dauer aller Vergiftungssymptome sowie der Zeitpunkt des Todes vermerkt.

Autopsie: Alle am Versuchsende getöteten Tiere wurden seziert, makroskopisch untersucht und der Befund registriert.

Auswertung: Von den Körpergewichten wurden die Mittelwerte (\bar{x}) berechnet. Die LD₅₀ wird im allgemeinen nach Litchfield und Wilcoxon bestimmt und mit 95 % Vertrauensbereich angegeben (J. Pharmacol. Exp. Ther. 96, 1949, 99).

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- 5 -

V Die Ergebnisse des Versuches wurden in der nachfolgenden Tabelle zusammengefaßt.

2-tert.-Butylcyclohexylacetat

Akute orale Toxizität (LD₅₀) für Ratten

Dosis mg/kg	Geschl.	Toxikol. Ergebnis	Eintritt des Todes innerh. von Std.	LD ₅₀ mg/kg
2510	männlich	0/5/5*		
	weiblich	3/5/5	24	
3160	männlich	1/5/5		
	weiblich	1/5/5	2 1/2	
3980	männlich	1/5/5		6100 (4519-8235)
	weiblich	1/5/5	24	Neigungsfunktion $S = 2,15$
5010	männlich	2/5/5		
	weiblich	2/5/5	28 1/2	
6310	männlich	3/5/5		
	weiblich	4/5/5	48	

*Anzahl der verendeten Tiere/Anzahl der Tiere mit Symptomen/Anzahl der eingesetzten Tiere

Körpergewichtsentwicklung (Mittelwerte) in g

Dosis mg/kg	vor Appl. (nüchtern)	24 Std. n. Appl.	1 Woche n. Appl.	2 Wochen n. Appl.	Gewichtszunahme
2510	192,3	206,4	228,3	247,9	55,6
3160	196,2	188,0	220,3	238,8	42,6
3980	195,4	182,9	209,3	228,1	32,7
5010	190,2	175,9	207,3	229,2	39,0
6310	196,8	194,3	231,3	250,3	53,5

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Die Behandlung war praktisch ohne Einfluß auf die Entwicklung der Körpergewichte.

15-30 Minuten nach der Verabreichung waren die Tiere sehr unruhig, hatten ein gesträubtes Fell und Atembeschwerden. Einige Tiere aller Dosisgruppen zeigten leichte bis starke Krämpfe, die sich von Stunde zu Stunde verstärkten. Im allgemeinen waren die Krämpfe nach 7-8 Stunden abgeklungen, nur in der höchsten Dosisgruppe zeigten 2 Tiere auch noch nach 24 Stunden diese Krämpfe. Bei den Krämpfen handelte es sich um tonisch-klonische Krämpfe, Spring-, Streck- und Rollkrämpfe. Gleichzeitig traten Opisthotonus, Exophthalmus, stark verkrampte Haltung mit Zittern, Wissbewegungen mit den Vorderpfoten zur Nase, plötzlich starker Blutaustritt aus Nase und Mund, Speichelfluß und Lautäußerungen auf. Zwischen den Krämpfen zeigten die Tiere Bauch- bzw. Seitenlage, verlangsamte Atmung, Zittern, Zuckungen, halb bzw. ganz geschlossene Augen, dunkle Augen und Straub'sches Phänomen. Von Mal zu Mal verstärkten und verlängerten sich die Krampfanfälle, wobei die Ruhepausen sich verkürzten. Nach 48-72 Stunden waren alle Tiere frei von Vergiftungssymptomen.

Post mortem ergaben die Sektionen bei einigen Tieren leichte bis starke Hyperämien der Magen- und Dünndarmschleimhäute, Verfärbungen von Nieren, Nebennieren und Lebern, Hyperämien der Lungen, Verätzungen der Magenschleimhäute, Verdickungen der Vormagenschleimhäute, Stauungslebern und Hyperämie des Bauchfells.

Die Sektionen am Versuchsende ergaben bei einigen Tieren herdförmige Verdickungen auf der Schleimhaut des Vormagens, vereinzelt fleckige Nieren, dunkelrot gefärbte Nebennieren sowie eine Hyperämie der Dünndarmschleimhaut.

Autor und Versuchsleiter

Ulrich Mürmann
(Dr. P. Mürmann)

Fachtierarzt für Pharmakologie und Toxikologie

Hüls AG
-WL Ps-

Copy No. 3
Marl, 10/20/1986

Report No. 0747

Acute oral toxicity of

2-tert.-butylcyclohexyl acetate

for rats

by
P. Mürmann

Until the results contained in this study are published, they may be used only with permission from Hüls AG, WL Ps. Reproduction of this report—even in excerpts—is not permitted.

- I -

I Summary:

An acute oral toxicity determination on male and female rats showed that the LD₅₀ of 2-tetra-butylcyclohexyl acetate is about 6,100 mg/kg of body weight. The treated animals were free of toxicity symptoms after 48-72 hr. The body weight changes were not influenced. The dissection at the end of the experiment showed, for some animals, focal thickenings on the forestomach mucosa, blotched kidneys in a few cases, dark red-colored adrenals and hyperemia of the small intestinal mucosae.

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II General:

Test substance: 2-tert.-butylcyclohexyl acetate

Chemical name: 2-tert.-butylcyclohexyl acetate

Test type: Acute oral toxicity (LD₅₀) for rats

Test number: 0747

Requested by: Dr. Korfmann, Org. Abt., Hüls AG, Marl

Test substance received on: 8/28/1986

Data sheet for test substance received on: 9/22/1986

Start of test: 9/29/1986

End of test: 10/15/1986

Study director: Dr. P. Mürmann

Responsible for carrying out the test: Ms. M. Porter, Ms. R. Hamphoff-Köhler

Report date: 10/20/1986

Archiving: Raw data, records, report and retained samples in appropriate rooms of Hüls AG, Building 2328

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III Physical and General Data on the Test Substance:

Physical state:	Liquid, cis-bonds tend to crystallize
Density (20°C):	0.941 g/cc
pH:	6.2
Appearance:	Colorless
Odor:	Characteristic
Melting point:	25-35°C
Boiling point (1013 mbar):	degradation above 204°C
Vapor pressure (112°C):	24 hPa
Flash point:	89°C
Purity:	Greater than 99%
Principal impurities:	
Date of manufacture:	August 1986
Batch No.:	Continuous manufacture
Special storage conditions:	
Necessary protective measures:	

IV Methods:

I) Experimental Animals and Their Housing:

Animal species, strain:	Rat, Bor: WISW (SPF TNO)
Bred by:	F. Winkelmann, 4799 Borcheln
Sex:	Male and female
Mean body weight:	194.2 g
Number of animals per dose:	10
Identification:	The animals within each group are unmistakably identified by staining the fur with picric acid
Housing:	1-5 animals in Makrolon cages, Type III
Acclimatization:	4-8 days
Feed:	R10 complete feed for rats, Ssniff Spezialfutter GmbH, D-4770 Soest, ad libitum
Water:	Tap water ad libitum
Room temperature:	20°C ± 1°C
Relative humidity:	60% ± 5%
Air change:	15 times/hour
Illumination:	12-hour light-dark cycle
Randomization:	Using a table of random numbers on distribution into the test cages

2) Experimental Procedure:

The test was conducted in accordance with the Guidelines for Testing of Chemicals Section 4: Health Effects, Method No. 401: Acute Oral Toxicity, of May 12, 1981, published by the Organization for Economic Cooperation and Development (OECD). The product was liquefied by heating in a water bath. Rats were fasted for 16 hours and then received a single dose by gavage (volume: 2.667–6.706 cc/kg).

To establish the dose, a preliminary test was conducted using a smaller number of animals from 9/25 to 10/9/1986.

Duration of the test: 14 days

3) Observations:

Body weights: The animals were weighed before the treatment and 1, 7 and 14 days after the treatment.

Symptoms: Up to 6 hours after treatment and then daily, the onset, type and duration of all toxicity symptoms and the time of death were recorded.

Autopsy: All of the animals killed at the end of the test were dissected, examined macroscopically and findings were recorded.

Evaluation: The mean body weights (\bar{x}) were calculated. The LD₅₀ is generally determined according to Litchfield and Wilcoxon and reported with 95% confidence limits (*J. Pharmacol. Exp. Ther.* **96**, 1949, 99).

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V The results of the test are summarized in the table below.

2-tert.-butylcyclohexyl acetate
Acute oral toxicity (LD₅₀) for rats

Dose mg/kg	Sex	Toxicological result	Death occurred within hours	LD ₅₀ mg/kg
2510	Male	0/5/5*	24	
	Female	3/5/5		
3160	Male	1/5/5	2 ½	6100 (4519-8235) slope function S = 2.16
	Female	1/5/5		
3980	Male	1/5/5	24	
	Female	1/5/5		
5010	Male	2/5/5	28 ½	
	Female	2/5/5		
6310	Male	3/5/5	48	
	Female	4/5/5		

*Number of animals that died/number of animals with symptoms/number of animals used

Changes in body weight (means) in g

Dose mg/kg	Before administration (fasting)	24 hours after administration	1 week after administration	2 weeks after administration	Weight gain
2510	192.3	206.4	228.3	247.9	55.6
3160	196.2	188.0	220.3	238.8	42.6
3980	195.4	182.9	209.3	228.1	32.7
5010	190.2	175.9	207.3	229.2	39.0
6310	196.8	194.3	231.3	250.3	53.5

The treatment had virtually no effect on body weight changes.

15–30 minutes after administration, the animals were very restless, had ruffled fur and breathing difficulties. Some animals of all dose groups showed slight to severe spasms, which intensified from hour to hour. Generally, the spasms subsided after 7–8 hours. Only in the highest dose group did two animals exhibit these after 24 hours. The spasms were tonic-clonic spasms, clonic spasms, extension spasms and rotatory spasms. Simultaneously, we observed opisthotonus, exophthalmus, pronounced crouched posture with shivering, wiping motions with the front paws at the nose, sudden severe bloody discharge from the nose and mouth, salivation and vocalizations. Between spasms, the animals showed prone or lateral position, slowed breathing, shivering, twitching, half-closed or completely closed eyes, dark eyes and Straub reaction. The spasmodic episodes were observed to intensify and become

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prolonged from time to time, with shortened rest periods. After 48-72 hours, all animals were free of intoxication symptoms.

Post-mortem, dissection of some animals revealed slight to severe hyperemia of the gastric and small-intestinal mucosae, discoloration of kidneys, adrenals and liver, hyperemia of the lungs, burns on the gastric mucosae, thickening of the forestomach mucosae, congestion in the liver and hyperemia of the abdominal skin.

In some animals, dissection at the end of the experiment revealed focal thickening on the forestomach mucosa, some cases of blotched kidneys, dark red adrenals and one case of hyperemia of the small-intestinal mucosa.

Author and Study Director

[signature]

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